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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,241	09/25/2003	Mark Korsten	6915-66816	8718

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

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05/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,241	KORSTEN, MARK	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,12-23,25,26 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,12-23,25,26 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/10/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Correction of Inventorship

In view of the papers filed April 10, 2007, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by **addition** of **William A. Bauman**.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Amendment

The amendment filed May 29, 2007 have been received and entered into the application.

Action Summary

The rejection of claims 1-26 under 35 U.S.C. 103(a) as being unpatentable over Ponec et al. (1999) in view of Vavilala et al. (1999) is being maintained for the reasons stated in the previous Office Action. However, the rejection is modified in this Office Action to exclude canceled claims and to address newly added claims.

Response to Arguments

Applicants' arguments filed May 29, 2007 have been fully considered but they are not persuasive. Applicants argue that neither Ponce et al. nor Vavilala et al. disclose, suggests or render obvious the chronic administration of a drug combination comprising an acetylcholinesterase inhibitor and an anti-cholinergic agent with a therapeutically effective amount to the patient having chronic intestinal pseudo-obstruction resulted from a spinal cord injury. This is not found to be persuasive because Ponce suggests concomitant treatment with neostigmine and the anticholinergic agent glycopyrrolate as been reported to diminish the central cholinergic effects of neostigmine without reducing the increase the colonic motility, thus, the combination of neostigmine and glycopyrrolate merits further study in patients with colonic pseudo-obstruction in general. (see page 141, left-hand side middle paragraph). No explicit teaching is necessary to have led the skilled worker to the particular pseudo-obstruction disease because Ponce suggests the concomitant treatment with neostigmine and glycopyrrolate can be used for treating colonic pseudo-

obstruction. Therefore, it would prompt the skilled worker to employ the combination in colonic pseudo-obstruction in general including chronic. KSR Int'l v.Teleflex Inc., 82 USPQ2d 1385, 1395 (2007). Applicants argue that chronic intestinal pseudo-obstruction (persistent, recurring intestinal pseudo-obstruction) is a very different condition from acute intestinal pseudo-obstruction (a relatively rapid onset, intense, short-term occurrence of intestinal pseudo-obstruction) having very different etiologies and treatment regimes. This is not found persuasive because in this case the etiologies overlap because the subject disclosed by Ponce et al. suffering from acute pseudo obstruction resulted from the spinal cord injury. (left-hand side page 139). Applicants argue that the unexpected results obtained using neostigmine and glycopyrrolate is documented in the specification. The specification specifically disclose the colonic response to neostigmine is not blunted by glycopyrrolate; and neostigmine and glycopyrrolate produced prompt and complete evacuation in 64% of subjects, higher than neostigmine alone (57%) . In addition, the combination of neostigmine and glycopyrrolate caused less bradycardia than neostigmine alone, and glycopyrrolate counteracts the respiratory side effects caused by neostigmine alone. This is not found to be persuasive because the data disclosed in the specification has been carefully reviewed and considered. However, it indicates that the treated subjects had SCI but it does not indicate that these subjects suffered from chronic pseudo obstruction. Therefore, Applicants' surprising and unexpected result is expected in view of cited art, Ponec et al's teaching that the administration of neostigmine to a patients with acute colonic pseudo-obstruction with spinal cord injury with paralysis (page 139,left-hand

side) and the teaching of concomitant treatment with neostigmine and the anticholinergic agent glycopyrrolate has been reported to diminish the central cholinergic effects of neostigmine without reducing the increase in colonic motility. (page 141, left-hand side middle paragraph). Further, the cited art suggest the combination of neostigmine and glycopyrrolate merits further study in patient with colonic pseudo-obstruction in general. Therefore, it would have been obvious to one of ordinary skill in the art to employ neostigmine together with glycopyrrolate for the treatment of colonic pseudo-obstruction including chronic with the suggestion of the employment of the combination in treatment of colonic pseudo-obstruction in general. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-9, 12-23, 25, 26 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ponec et al. (1999) of record in view of Vavilala et al. (1999) of record.

Ponec et al. teach that neostigmine is useful for the treatment of acute colonic pseudo-obstruction. (title). Ponec et al. teach that in patients with acute colonic pseudo-obstruction who have not had a response to conservative therapy, treatment with neostigmine rapidly decompresses the colon. (page 137, left-hand column under Conclusions). Ponec et al. teach that side effect of neostigmine of symptomatic bradycardia developed in two patients and was treated with atropine. (page 137 under Results). Ponec et al. teach that patients with acute colonic pseudo-obstruction received 2.0 mg of neostigmine intravenously over a period of three to five minutes. This amount overlap with Applicant's amount set forth in claims 7-9 and 23. Ponec et al. teach that acute colonic pseudo-obstruction may develop after surgery or severe illness and that colonoscopic decompression is needed to prevent ischemia and perforation of the bowel. (abstract).

Ponec et al. lack glycopyrrolate for the treatment of pseudo-obstruction and various medical conditions resulted in pseudo-obstruction, other routes of administration, and dosing frequencies.

Vavilala et al. teach that neostigmine for acute colonic pseudo-obstruction rapidly decompresses the colon in patients with acute colonic pseudo-obstruction but causes bradycardia. Vavilala et al. teach that the bradycardia is a well-recognized and important complication of neostigmine therapy. Vavilala et al. teach that the use of neostigmine is always accompanied by administration of an antimuscarinic anticholinergic agent such as atropine or glycopyrrolate to reverse this effect. (abstract).

It would have been obvious to one ordinary skill in the art at time the invention was made to combine neostigmine and glycopyrrolate in bowel care or to combine to treat pseudo-obstruction in a patient because neostigmine is useful for the treatment of pseudo-obstruction by rapidly decompressing the colon and because glycopyrrolate is useful for preventing the development of adverse effect of neostigmine such as bradycardia. One would have been motivated to combine neostigmine and glycopyrrolate in a single component in order to achieve rapid decompression of colon in patients suffering from pseudo-obstruction without the complications of bradycardia, well recognized and important adverse effect of neostigmine. One would have been motivated to make such a modification in order to prevent well-recognized and important complication well-recognized in neostigmine therapy. Moreover, it is well known by Vavilala et al. that neostigmine is always accompanied by the administration of atropine or glycopyrrolate to reverse the adverse effect result from neostigmine. The amounts of active agent (glycopyrrolate) to be used, the pharmaceutical forms, e.g., tablets, etc; route of administration (intranasal) and cause of resulted condition are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration. One of ordinary skill in the art would optimize the dosage of glycopyrrolate taught by Vavilala in the obvious combination in order to customize the dosage needed based on the patients physical and medical profile. Furthermore, there is an expectation of successfully treating pseudo-obstruction in a patient regardless of the cause because the

neostigmine comprising therapy is effective for treating such condition as taught by Ponec et al.

Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
May 8, 2008